In the Specification:

On page 2, please amend the first paragraph as follows:

CROSS-REFERENCE TO RELATED APPLICATION

This application is a continuation-in-part of U.S. patent application number 08/900,117 ~~tiled~~ filed on July 25,1997, now U.S. Patent No. 6,326,485 which claims priority to ~~is a continuation in part of~~ U.S. Provisional application number 60/023,345 ~~tiled~~ filed on July 26, 1996, the contents of which are incorporated herein.

On page 6, please amend the last paragraph as follows:

The polymerase chain reaction ("PCR") and other probe based assays require a specific DNA sequence as a target. In diagnostic applications it is desirable that the DNA target sequence has a high copy number so as to increase the likelihood of detection at low levels of infection. Most organisms contain multiple copies of the regions that code for the ribosomal RNAs ("rRNA"). Usually RNA genes are organized in clusters comprising the following sequences shown schematically in Fig. 1: 5.0S region, non-transcribed spacer ("NTS"), small subunit ~~("1S5U")~~ ("SSU") region, internal transcribed spacer 1 ~~("ITS1")~~ ("ITS"), 5.8S gene, internal transcribed spacer 2 ("1T52"), and large subunit ("LSU") region. The NTS separates transcription units but is not represented in the mature RNA products. Although this part of the molecule may not be important in terms of virulence or parasite proliferation, it is used, in accordance with the present invention, as a marker to distinguish between species and types. Coding regions of the rRNA genes are evolutionarily conserved, whereas the NTS is more variable and can differ significantly between even closely related species. The amplification primers and probes of the invention are based on the NTS domain of *P. marinus* and other species of this genus. Since each eukaryotic microorganism has its own unique, species specific NTS sequence, the assay according to the present invention can be used to detect the genomic "fingerprint" of any target microorganism in a sample being tested. In short, to create an assay for a particular microorganism one needs to (i) isolate and sequence the NTS region for that species, and (ii) design an oligonucleotide probe or primers that will preferentially hybridize to the unique NTS.

On page 9, please amend the second full paragraph as follows:

In addition to *P. marinus, Perkinsus*- like organisms of unknown virulence have been detected in bivalve species sympatric with *C. virginica* (Andrews 1954). For example, production of zoospores seawater without preincubation in FTM (Kleinschuster and Swink 1993; Perkins 1988), morphological features of the trophozoite in host tissue (Perkins 1988), and partial sequences of the SSU and ITS regions reported earlier (Coss et al. 1997) indicated that *Perkinsus* isolates from the baltic clam *Macoma balthica* may be a different species from *P. marinus.* The identity and host specificity of the various *Perkinsus* species described in sympatric mollusk species in Chesapeake Bay, and the possibility that these may constitute alternate hosts or reservoir species for *P. marinus* has received limited ~~affention~~ attention (Coss et al. 1997; McLaughlin and Faisal 1998; Coss, Robledo, and Vasta, in press). Accordingly, questions about the presence of *P. marinus* in non-oyster bivalves, as well as other *Perkinsus* species infecting *C. virginica,* are addressed in this application.

On page 11, please amend the "Brief Description of the Drawings" as follows:

Fig. 1 is a schematic diagram of an rRNA gene cluster.

Fig. 2 is the nucleotide sequence of the nontranscribed space (NTS) from *Perkinsus marinus* (SEQ ID NO.1).

Fig. 3 is the nucleotide sequence of the NTS of rRNA of *P. andrewsi,* isolated from *Macoma balthic* (SEQ ID NO.2).

Fig. 4 is the nucleotide sequence of the NTS of rRNA of *Perkinsus mackini* isolated from *Mercenaria mercenary* (SEQ ID NO. 3).

Fig. 5 lists representative sets of primers used for diagnosis of *Perkinsus marinus, Perkinsus andrewsi,* and primers for *Perkinsus marinus* typing (SEQ ID NOs. 4, 5. 6, 7, 10, 11, 20, 21, 22 and 23).

Fig. 6 is an agarose gel electrophoresis of amplified products of PCR demonstrating species-specificity of *P. marinus* diagnostic primers. Amplification of DNA with *P. marinus* diagnostic primers (d) only occurred with *P. marinus* samples. However, PCR with actin primers (a) amplified all samples. *P.* sp. (1) *Perkinsus* sp. from *Anadara trapezia,* P. o. P. *olseni* from *Haliotis laeviagata,* P.a. *P. atlanticus* from *Ruditapes decussatus,* P.m. *P. marinus* from *Crassostrea virginica.* M. 123 bp DNA ladder.

Fig. 7 are agarose gel electrophoresis of amplified products of PCR demonstrating the sensitivity of *P. marinus* diagnostic primers. Using this methodology as few as one cell was detected. Three samples

(X 3) were used for 1,2,5,8, and 10 cells.

Fig. 8 is an agarose gel electrophoresis of PCR products of different *Perkinsus* isolates using *P. marinus* diagnostic primers (a) and primers derived *Perkinsus* sp. isolated *Macoma balthica* (b). *1. Perkinsus* sp. from *Mercenaria mercenaria* 2. *Perkinsus* sp. from *Macoma balthica,* 3. *P. marinus* from *Crassostrea virginica,* 4. Negative controls, M. 123 bp DNA ladder.

Fig. 9 is amplification of the *Perkinsus marinus* DNA target using a known amount of total *P. marinus* DNA in a 10X serial dilution with a constant level of oyster genomic DNA (1 μg/μl). A. Ethidium bromide visualization of the resolving gel. B. Southern blot of the above gel. C. Dot-blot hybridization of PCR amplification.

Fig. 10 is a ribosomal DNA nucleotide sequence of the non-transcribed spacer (NTS) domain from *Perkinsus marinus* Type I (SEQ ID NO. 24) and Type II (SEQ ID NO. 25). Nucleotides shown in boldface indicate differences between *P. marinus* types.

Fig. 11 is an ethidium bromide stained agarose gel electrophoresis of PCR products generated by amplification of DNA derived from oysters *(Crassostrea virginica)* infected with *Perkinsus marinus.* Lanes 1 to 5 using primers PM5/PM7 specific for *P.marinus* type 1 (lane a) and primers PM6/PM8 specific for *P. marinus* type II (lane b). M. 123 bp DNA ladder. (+) control *P. marinus* type II. Note the presence of bands corresponding to both *Perkinsus* types in the same oyster in samples #2 and #3.

Fig. 12 is an agarose gel showing the patterns of *Perkinsus marinus* types after *Spe* 1 digestion of PCR amplified products. *P. marinus* type I (samples #1 and #2) and *P. marinus* type II (sample #3). Sample with enzyme (lane a). Sample without enzyme (lane b).

Fig. 13 is a chart showing the distribution of *Perkinsus marinus* types in samples form Maryland, Florida, and Louisiana.

Fig. 14 is a chart showing the standard curves of the dot blot and Southern blot of the amplified *Perkinsus marinus* DNA target as a function of total *P. marinus* DNA that was used in the amplification.

Fig. 15 is an agarose gel electrophoresis of amplified products of PCR demonstrating the presence of *Perkinsus marinus* is samples obtained from the mantle of *Crassostrea virginica* from Louisiana (+): positive control, (-) negative control.

Fig. 16 is an agarose gel electrophoresis of amplified products of PCR demonstrating the presence of *Perkinsus marinus* in samples obtained from *Macoma balthica* from Rhode River. Lanes 1-7: DNA from *M. balthica* individuals, (+): positive control, (-): negative control.

Fig. 17 is the nucleotide sequences of the NTS of rRNA of *P. atlanticus* (SEQ ID NO.8)..

Fig. 18a-b is the nucleotide sequence of the SSU rRNA of *P. Andrewsi* (SEQ ID NO.17).

Fig. 19 is the nucleotide sequence of the ITS1-5.8.S-ITS2 regions of *P.andrewsi* (SEQ ID NO.16).

Figs. 20-21 list representative sets of primers for *P. marinus, P. andrewsi, P. makinsus* typing and "generic primers" (SEQ ID NOs. 4, 5, 8, 9, 10, 1`1, 12 13 and 19)..

On page 21, please amend the last paragraph as follows:

As further described in the following examples, the sequence of NTS region from *P. atlanticus* isolated from Galicia, Spain, has been cloned and ~~sequences~~ sequenced and is shown in Fig. 17 (SEQ ID NO. 8). The most suitable pair of *P. atlanticus-specific* primers consisted of forward sequence (PA69OF, 5' ATG CTA TGG TTG GTT GCG GAC C 3') (SEQ ID NO. 8) and a reverse sequence (PA69OR, 5' GTA GCA AGC CGT AGA ACA GC 3') (SEQ ID NO. 9) that would result in amplicon of 690 bp is shown in Fig. 20. *P. atlanticus* DNA was not amplified by using the PCR-based assay specific for *P. marinus*. Some details of the method may be found in the publication by Robledo et al. (2000), "Characterization ~~Characterization~~ of the ribosomal RNA locus of *Perkinsus atlanticus* and development of a polymerase chain reaction based diagnostic assay" [2000], *Journal of Parasitology* 86 (5): 972-978.

On page 41, please amend the last paragraph as follows:

In order to identify *Perkinsus* type, two methods of differentiation can be applied: (a) by PCR, using newly designed sets of primers with specific amplification of individual *P. marinus* types and (b) restriction mapping. PCR using the PM5/PM7 primers (SEQ ID NOs. 20 and 21) amplified *P. marinus* type I (SEQ ID NO. 24) and PM6/PM8 primers (SEQ ID NOs. 22 and 23) amplifies *P. marinus* type II (Fig. 10 (SEQ ID NO. 25)) exclusively, thus establishing specificity of the primers. The PCR reaction mixture used with the new primers was as above (Example 3B). The annealing temperature was 60°C instead of 58°C as used for the PCR diagnostic assay in order to increase the specificity (Fig. 11). The original diagnostic primers (not type-specifies) produced a 307 bp PCR product digestible with *Spe*I in the case of Type I (SEQ ID NO. 24), whose sequence contains the restriction site, but not Type II (SEQ ID NO. 25), whose sequence does not have the site. Restriction enzyme digestion was carried out using the *Spe*I (ACTAGT) enzyme. The enzyme mix was added to a final volume of 20µl following the

manufacture recommendations (GIBCOBRL) in the presence of 200 ng of PCR products. After 3h of incubations at 37°C, the digested products were run on a 1.5% agarose gel in the presence of ethidium bromide to resolve digested PCR fragments. One band was 245 bp and the other 62 bp (Fig. 12). Consequently, both specific PCR and restriction digestion can be used in the future for *P. marinus* type identification. In vitro culture methods will permit investigation of other genes that probably are more relevant for the virulence and pathogenicity of *P. marinus*. Restriction maps will also permit the identification of specific regions of the *P. marinus* genome that vary between types and specific genes present in only one type, possibly relevant to virulence and pathogenicity.

Amendment of Claims

1. (Currently amended) An oligonucleotide which hybridizes to a non-transcribed spacer sequence between rRNA genes of an organism of the genus *Perkinsus* being assayed, wherein said organism of genus *Perkinsus* contains a nucleotide base sequence selected from the group consisting of the sequences of SEQ ID NO. 18. ~~SEQ ID NOs. 1, 2, 3, and 18~~.

2. (Currently amended) A method of making an oligonucleotide for use in assaying a target organism of the genus *Perkinsus* comprising the steps of:

(i) extracting DNA from said target organism

(ii) isolating from said DNA a non-transcribed spacer sequence flanked by rRNA genes;

(iii) sequencing said non-transcribed spacer sequence; and

(iv) synthesizing ~~and~~ an oligonucleotide of the non-transcribed space sequence having a nucleic acid sequence of SEQ ID NO. 18.

3. (Currently amended) A kit for determining the identity of species of a microorganism of the genus *Perkinsus,* comprising a container having outwardly directed PCR primer pairs to a non-transcribed spacer sequence flanked by rRNA genes, said primer pairs, having a nucleic acid sequence selected from the group consisting of sequences of SEQ ID NO. 18. ~~SEQ ID NOs. 1, 2, 3, and 18~~.

4. (Original) The oligonucleotide of claim 1 wherein said organism is *Perkinsus atlanticus*.

5.-8. (Cancelled)

9. (Original) The oligonucleotide of claim 1 wherein said oligonucleotide is one of a pair of PCR primers, or complement thereof.

10. (Original) The oligonucleotide of claim 9, wherein said oligonucleotide is between about 10 to 35 nucleotides in length.

11. (Original) The oligonucleotide of claim 9, wherein said oligonucleotide is between about 15 to 24 nucleotides in length.

12. (Currently amended) The oligonucleotide of claim 9 wherein said PCR primers or complement thereof are selected from the group consisting of:

~~CAC TTG TAT TGT GAA GCA CCC (SEQ ID NO. 4)~~
~~TTG GTG ACA TCT CCA AAT GAC (SEQ ID NO. 5)~~
ATG CTA TGG TTG GTT GCG GAC C ~~(SEQ ID NO. 6)~~ (SEQ ID NO. 8)
GTA GCA AGC CGT AGA ACA GC ~~(SEQ ID NO 7)~~ (SEQ ID NO. 9)
~~AAG TCG AAT TGG AGG CGT GGT GAC (SEQ ID NO. 10)~~
~~ATT GTG TAA CCA CCC CAG GC (SEQ ID NO. 11)~~
TAG TAC CCG CTC ATT GTG G ~~(SEQ ID NO. 20)~~ (SEQ ID NO. 12)
TGC AAT GCT TGC GAG CT ~~(SEQ ID NO. 21)~~ (SEQ ID NO. 13)
AGT TGG ATT TCT GCC TTG GGC G ~~(SEQ ID NO. 22)~~ (SEQ ID NO. 14); and
ACC AGG TCC AGA CAT AGG AAG G ~~(SEQ ID NO. 24)~~ (SEQ ID NO. 15).

13. (Previously presented) The oligonucleotide of claim 1, wherein said oligonucleotide is detectably labeled.

14. (Cancelled)

15. (Previously presented) The oligonucleotide of claim 1, wherein said nucleic acid sequence is exactly complementary to said non-transcribed spacer sequence.

16. (Previously presented) The method of claim 2, wherein said non-transcribed spacer sequence is isolated by amplifying said nontranscribed spacer sequence using primers, or complement thereof that preferentially hybridize to said flanking rRNA genes.

17. (Previously presented) The method of claim 2, wherein said nontranscribed spacer is isolated by the steps of digesting said DNA with restriction enzyme, creating a library, and identifying said nontranscribed spacer sequences within said library using a probe specific for one of said rRNA genes.

18. (Original) The method of claim 2, wherein said oligonucleotide is one of a pair of PCR

primers or complement thereof.

19. (Cancelled)

20. (Currently amended) The kit of claim 3 wherein said PCR primers pairs or complement thereof are selected from the group consisting of ~~SEQ ID NO. 4, SEQ ID NO. 5,~~ SEQ ID NO. 8, SEQ ID NO. 9, ~~SEQ ID NO. 10, SEQ ID NO. 11,~~ SEQ ID NO. 12, SEQ ID NO. 13, SEQ ID NO. 14, SEQ ID NO. 15 and SEQ ID NO. 19.

21. (New) An oligonucleotide which hybridizes to a non-transcribed spacer sequence between rRNA genes of an organism of the genus *Perkinsus* being assayed, wherein said organism of genus *Perkinsus* contains a nucleotide base sequence selected from the group consisting of the sequences of SEQ ID NOs. 1, 2, and 3.

22. (New) The oligonucleotide of claim 21 wherein said organism is *Perkinsus Andrews* comprising SEQ ID NO. 2.

23. (New) The oligonucleotide of claim 21, wherein said organism is *Perkinsus mackin* comprising SEQ ID NO. 3.

24. (New) The oligonucleotide of claim 21 wherein said oligonucleotide is one of a pair of PCR primers, or complement thereof.

25. (New) The oligonucleotide of claim 24, wherein said oligonucleotide is between about 10 to 35 nucleotides in length.

26. (New) The oligonucleotide of claim 24, wherein said oligonucleotide is between about 15 to 24 nucleotides in length.

27. (New) The oligonucleotide of claim 21 wherein said PCR primers or complement thereof are selected from the group consisting of:

CAC TTG TAT TGT GAA GCA CCC (SEQ ID NO. 4);
TTG GTG ACA TCT CCA AAT GAC (SEQ ID NO. 5);
AAG TCG AAT TGG AGG CGT GGT GAC (SEQ ID NO. 10); and
ATT GTG TAA CCA CCC CAG GC (SEQ ID NO. 11).

28. (New) The oligonucleotide of claim 21, wherein said nucleotide base sequence has type I or type II NTS sequences of (SEQ ID NOs. 24 or 25).

29. (New) A kit for determining the identity of species of a microorganism of the genus *Perkinsus,* comprising a container having outwardly directed PCR primer pairs to a non-transcribed spacer sequence flanked by rRNA genes, said primer pairs, having a nucleic acid sequence selected from the group consisting of sequences of SEQ ID NOs. 1, 2 and 3.

30. (New) The kit of claim 29 wherein said PCR primers pairs or complement thereof are selected from the group consisting of SEQ ID NO. 10 and SEQ ID NO. 11.

31. (New) A kit for determining the identity of species of a microorganism of the genus *Perkinsus,* comprising a container having outwardly directed PCR primer pairs to a non-transcribed spacer sequence flanked by rRNA genes, said primer pairs, having a nucleic acid sequence selected from the group consisting of sequences of SEQ ID NO. 12, SEQ ID NO. 13, SEQ ID NO. 14, SEQ ID NO. 15 and SEQ ID NO. 19.

REMARKS

Rejection of Claims and Traversal Thereof

In the May 2, 2003 Office Action,

claims 2, 3, 5, 12 and 14-20 were rejected under 35 U.S.C. §112, second paragraph;

claims 1, 4-12 and 14-15 were rejected under 35 U.S.C. §102(b) as being anticipated by Robledo (Robledo et al. (1999) Nucleotide Sequence Variability in the Nontranscribed Spacer of the rRNA Locus in the Oyster Parasite *Perkinsus marinus*. J. Parasitol. 85:650-656)(hereinafter Robledo 1);

claims 1, 4-15 are rejected under U.S.C. §102(b) as being anticipated by Marsh (Marsh, et al. (1995) A semiquantitative PCR Assay for Assessing Perkinsus Marinus Infections in the Eastern Oyster, Crassostrea Virginica, J. Parasitol. 81(14); 577-583)(hereinafter Marsh);

claims 1, 2 and 4-18 were rejected under 35 U.S.C. §102(a) as being anticipated by Robledo (Robledo, J.A., C.A. Coss and G.R. Vasta (2000) Characterization of the Ribosomal RNA Locus of *Perkinsus atlanticus* and Development of a Polymerase Chain Reaction-Based Diagnostic Assay. J. Parasitol. **86**:972-978) (hereinafter Robledo 2);

claims 1, 4-9, 14 and 15 were rejected under 35 U.S.C. §102(a) as being anticipated by Robledo (GenBank Accession No. AF140295/NCBI Database, April 17, 2000) (hereinafter Robledo 3);

claim 13 was rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 1 in view of Stokes (Stokes, N.A. and Burreson, E.M. 1995. A sensitive and Specific DNA Probe for the Oyster Pathogen Haplosporidium Nelsoni. J. Euk. Microbiol. 42: 350-357);

claim 13 was rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 2 in view of Stokes;

claims 3, 19 and 20 were rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 1 in view of the Stratagene Catalog (1988);

claims 3, 19 and 20 were rejected under 35 U.S.C. §103(a) as being unpatentable over Marsh (Marsh, A.G., J.D. Gauthier, G.R. Vasta. 1995. A semiquantitative PCR assay for assessing Perkinsus marinus infections in the eastern oyster, Crassostrea virginica. J. Parasitol., 81: 577-583) in view of the Stratagene Catalog (1988);

claims 3, 19 and 20 were rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 2 in view of the Stratagene Catalog (1988);

claims 2, 9-11, 13 and 16-18 were rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 3 in view of the Marsh;

claims 3 and 19 were rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 3 in view of Marsh and in further view of the Stratagene Catalog (1988); and

claims 1 and 3-20 were rejected under the judicially created doctrine of obviousness double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,326,485.

These rejections are traversed and reconsideration of the patentability of the pending claims is requested in light of the following remarks.

Claims

Claims 1-4 as amended recite SEQ ID NO. 18 and this sequence is not disclosed in Robledo 1 (AX Reference) or Marsh (AP Reference), and Robledo 2 and 3 are removed as prior art by enclosed Declaration by Dr. Vasta.

Claims 5-8 are cancelled herein.

Claims 9-11 as amended recite SEQ ID NO. 18, which is not disclosed in Robledo 1 (AX Reference) or Marsh (AP Reference), and Robledo 2 and 3 are removed as prior art by enclosed Declaration by Dr. Vasta.

Claim 12 as amended recite SEQ ID NOs. 18, 8, 9, 12, 13, 14, and 15 and these sequences are not disclosed in Robledo 1 (AX Reference) or Marsh (AP Reference), and Robledo 2 and 3 are removed as prior art by enclosed Declaration by Dr. Vasta.

Claim 13 as amended recite SEQ ID NO. 18 which is not disclosed in Robledo 1 (AX Reference) or Marsh (AP Reference), and Robledo 2 and 3 are removed as prior art by enclosed Declaration by Dr. Vasta.

Claim 14 is cancelled herein.

Claims 15-18 as amended recite SEQ ID NO. 18 and this sequence is not disclosed in Robledo 1 (AX Reference) or Marsh (AP Reference), and Robledo 2 and 3 are removed as prior art by enclosed Declaration by Dr. Vasta.

Claim 19 is cancelled herein.

Claim 20 as amended recite SEQ ID NOs. 18, 8, 9, 12, 13, 14, 15, and 19 and these sequences are not disclosed in Robledo 1 (AX Reference) or Marsh (AP Reference), Robledo 2 and 3 are removed as prior art by enclosed Declaration by Dr. Vasta.

Claims 21-30 (Priority date of July 25, 1997) as written recite SEQ ID NOs. 1, 2, 3, 4, 5, 10, 11, 24 and 25 are disclosed in parent application filed on July 25, 1997.

Claim 31 as written recites SEQ ID NOs. 12, 13, 14, 15 and 19 and these sequences are not disclosed in Robledo 1 (AX Reference) or Marsh (AP Reference), and Robledo 2 and 3 are removed as prior art by enclosed Declaration by Dr. Vasta.

Rejection under 35 U.S.C. §112, Second Paragraph

Claims 2, 3, 5, 12 and 14-20 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. Applicants have amended claims 2, 3, 5, 12 and 14-20 thereby obviating this rejection under §112, second paragraph.

Rejection under 35 U.S.C. §102(b)

I. Claims 1, 4-12 and 14-15 were rejected under 35 U.S.C. §102(b) as being anticipated by Robledo (Robledo et al. (1999) Nucleotide Sequence Variability in the Nontranscribed Spacer of the rRNA Locus in the Oyster Parasite *Perkinsus marinus*. J. Parasitol. **85**:650-656)(hereinafter Robledo 1). Applicants traverse this rejection.

Applicants have amended independent claim 1, and claims depending therefrom to recite SEQ ID NO: 18, which is the nucleotide sequence of the NTS of rRNA of P. atlanticus. The Robledo 1 reference does not disclose SEQ ID NO. 18, and as such, does not anticipate claims 1, 4-12 and 14-15. Claim 12 recites SEQ ID NOs. 18, 8, 9, 12, 13, 14, and 15, and these sequences are not disclosed in the Robledo 1 reference. Thus, Robledo 1 does not anticipate the presently claimed invention because it does not disclose each and every element of the presently claimed invention. The Robledo 1 reference does not meet the statutory requirements of an anticipating reference because each and every element of the claimed invention is not found in the cited reference. Applicants request the rejection under 35 U.S.C. §102(b) be withdrawn.

II. Claims 1, 4-15 are rejected under U.S.C. §102(b) as being anticipated by Marsh (Marsh, et al. (1995) A semiquantitative PCR Assay for Assessing Perkinsus Marinus Infections in the Eastern Oyster, Crassostrea Virginica, J. Parasitol. 81(14)/; 577-583)(hereinafter Marsh). Applicants traverse this rejection.

Applicants have amended independent claim 1, and claims depending therefrom to recite SEQ ID NO: 18, which is the nucleotide sequence of the NTS of rRNA of P. atlanticus. The Marsh reference does not disclose SEQ ID NO. 18, and as such, does not anticipate claims 1, 4-12 and 14-15. Claim 12 recites SEQ ID NOs. 18, 8, 9, 12, 13, 14, and 15, and these sequences are not disclosed in the Marsh reference. Thus, Marsh does not anticipate the presently claimed invention because it does not disclose each and every element of the presently claimed invention. The Marsh reference does not meet the statutory

requirements of an anticipating reference because each and every element of the claimed invention is not found in the cited reference. Applicants request the rejection under 35 U.S.C. §102(b) be withdrawn.

Rejection under 35 U.S.C. §102(a)

I. Claims 1, 2 and 4-18 were rejected under 35 U.S.C. §102(a) as being anticipated by Robledo (Robledo, J.A., C.A. Coss and G.R. Vasta (2000) Characterization of the Ribosomal RNA Locus of *Perkinsus atlanticus* and Development of a Polymerase Chain Reaction-Based Diagnostic Assay. J. Parasitol. **86**:972-978) (hereinafter Robledo 2). Applicants traverse this rejection.

Applicants have included herewith a Declaration executed by Dr. Vasta, attesting to the fact that he and his co-inventors were all co-authors of the cited publication (Robledo 2) and that the cited publication was describing their own work. The execution of this declaration is sufficient to remove the publication as a reference under 35 USC 102(a).

II. Claims 1, 4-9, 14 and 15 were rejected under 35 U.S.C. §102(a) as being anticipated by Robledo (GenBank Accession No. AF140295/NCBI Database, April 17, 2000) (hereinafter Robledo 3). Applicants traverse this rejection.

Applicants have included herewith a Declaration executed by Dr. Vasta, attesting to the fact that he and his co-inventors were all co-authors of the cited publication (Robledo 2) and that the cited publication was describing their own work. The execution of this declaration is sufficient to remove the publication as a reference under 35 USC 102(a).

Rejection under 35 U.S.C. §103(a)

I. Claim 13 was rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 1 in view of Stokes. Applicants traverse this rejection.

The Office is relying on the teachings of the primary reference for teaching isolated nucleic acids comprising the NTS region of the *Perkinsus marinus*. Stokes is cited for teaching labeling of nucleic acid

probes. However, applicants have amended claim 1 and all claims depending therefrom to recite SEQ ID NO: 18, which is the nucleotide sequence of the NTS of rRNA of *P. atlanticus*.

Applicants submit that none of the above-remaining prior art references render applicants' claimed invention *prima facie* obvious.

According to MPEP 706.02(j):

> "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir 1991)."

Claim 13 relates to detectably labeling SEQ ID NO. 18, which is the nucleotide sequence of the NTS of rRNA of *P. atlanticus*. Applicants submit that there is no teaching or suggestion in either reference or the combination thereof to use SEQ ID NO: 18 in an assay. Clearly, even if the references are combined, each and every element contained in the claim is not disclosed, specifically SEQ ID NO. 18, and thus, the combination is insufficient to establish obviousness. Applicants request that the rejection of claim 13 under 35 USC §103(a) be withdrawn.

II. Claim 13 was rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 2 in view of Stokes. Applicants traverse this rejection.

The Office is relying on the teachings of the primary reference for teaching isolated nucleic acids comprising the NTS region of the *Perkinsus atlanticus*. Stokes is cited for teaching labeling of nucleic acid probes. However, by virtue of the concurrently submitted Declaration by Dr. Vasta, Robledo 2 is not prior art to the instant claimed invention -- the combination therefore fails as a tenable basis for rejecting claim 13 because all elements of applicants' claimed invention are not disclosed, taught or suggested.

III. Claims 3, 19 and 20 were rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 1 or Marsh in view of the Stratagene Catalog (1988). Applicants traverse these rejections.

The Office is relying on the teachings of the primary references Robledo 1 or Marsh for teaching isolated nucleic acids comprising the NTS region of the *Perkinsus marinus*. The Stratagene Catalog is cited for teaching the general concept of kits for performing nucleic acid hybridization methods. However, applicants have amended claim 1 and all claims depending therefrom to recite SEQ ID NO: 18, which is the nucleotide sequence of the NTS of rRNA of *P. atlanticus*. Applicants submit that there is no teaching or suggestion in either reference or the combination thereof to use SEQ ID NO: 18 in an assay kit. Thus, even if the references are combined, each and every element contained in the claims is not disclosed, specifically SEQ ID NO. 18, and thus the combination is insufficient to establish obviousness. Applicants request that the rejection of claims 3, 19 and 20 under 35 USC §103(a) be withdrawn.

IV. Claims 3, 19 and 20 were rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 2 in view of the Stratagene Catalog (1988). Applicants traverse this rejection.

The Office is relying on the teachings of the primary references Robledo 2 for teaching isolated nucleic acids comprising the NTS region of the *Perkinsus atlanticus*. The Stratagene Catalog is cited for teaching the general concept of kits for performing nucleic acid hybridization methods. However, by virtue of the concurrently submitted Declaration by Dr. Vasta, Robledo 2 is not prior art to the instant claimed invention -- the combination therefore fails as a tenable basis for rejecting claims 3, 19 and 20 because all elements of applicants' claimed invention are not disclosed, taught or suggested. Withdrawal of rejection under 35 USC 103(a) is requested.

V. Claims 2, 9-11, 13 and 16-18 were rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 3 in view of the Marsh. Applicants traverse this rejection.

The Office is relying on the teachings of the primary references Robledo 3 for teaching isolated nucleic acids comprising the NTS region of the *Perkinsus atlanticus*. Marsh is cited for teaching labeling of the NTS sequences so that they may be used for probes. However, by virtue of the concurrently submitted Declaration by Dr. Vasta, Robledo 3 is not prior art to the instant claimed invention -- the combination therefore fails as a tenable basis for rejecting claims 2, 9-11, 13 and 16-18 because all elements of

applicants' claimed invention are not disclosed, taught or suggested. Withdrawal of rejection under 35 USC 103(a) is requested.

VI. Claims 3 and 19 were rejected under 35 U.S.C. §103(a) as being unpatentable over Robledo 3 in view of Marsh and in further view of the Stratagene Catalog (1988). Applicants traverse this rejection.

The Office is relying on the teachings of the combination of Robledo 3 and Marsh as above and the Stratagene Catalog for teaching the use of a kit. However, by virtue of the concurrently submitted Declaration by Dr. Vasta, Robledo 3 is not prior art to the instant claimed invention -- the combination therefore fails as a tenable basis for rejecting claims 3 and 19 because all elements of applicants' claimed invention are not disclosed, taught or suggested. Withdrawal of rejection under 35 USC 103(a) is requested.

Filing of Terminal Disclaimer to Overcome Double Patenting Rejection of Claims 1 and 3-20

In response to the rejection of claims 1 and 3-20 on judicially created obviousness-type double patenting grounds, on the basis of commonly owned and assigned U.S. Patent 6,326,485 a Terminal Disclaimer is enclosed and submitted herewith, overcoming such rejection. Accordingly, the rejection of currently pending claims on judicially created obviousness-type double patenting grounds is overcome by the filing of the Terminal Disclaimer and applicants therefore request that the rejection based on judicially created obviousness-type double patenting be withdrawn.

Petition for Extension of Time/Fees Payable

The applicants hereby petition for a two (2) month extension of time, extending the deadline for responding to the May 30, 2003 Office Action from August 30, 2003 to October 30, 2003. The entry of this petition results in a petition fee of $ 210.00. Applicants are filing herewith a Terminal Disclaimer and entry of this Terminal Disclaimer results in a fee of $55.00. Applicants introduced eleven (11) additional claims, three (3) of which are independent claims. However, applicants cancelled six (6) claims herein. Thus, an additional fee of $439.00 is enclosed for five (5) additional independent claims.

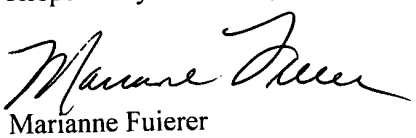
Submitted herewith is a check in the amount of $421.00 which includes payment of the fee for filing of a Terminal Disclaimer in the amount of $55.00, petition fee for a two month extension of $210.00 and fee for additional claims of $174.00.

The U.S. Patent and Trademark Office is hereby authorized to charge any additional amount necessary to the entry of this amendment, and to credit any excess payment, to Deposit Account No. 08-3284 of Intellectual Property/Technology Law.

Conclusion

The pending claims, as now amended, patentably distinguish over the prior art, and in view of the forgoing remarks, it is respectfully requested that all rejections be withdrawn thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Myers is requested to contact the undersigned attorney at (919) 419-9350 to resolve same.

Respectfully submitted,



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